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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,556	01/10/2002	Wilfried Lubisch	33827-US-009	2746
32116	7590	02/01/2005	EXAMINER	
WOOD, PHILLIPS, KATZ, CLARK & MORTIMER 500 W. MADISON STREET SUITE 3800 CHICAGO, IL 60661			COLEMAN, BRENDA LIBBY	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 02/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/041,556

Applicant(s)

LUBISCH ET AL.

Examiner

Brenda L. Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 and 10-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-8 and 10-13 are pending in the application.

This action is in response to applicant's amendment filed October 25, 2004.

Claim 1, 6, 10 and 12 were amended.

### ***Response to Amendment***

Applicant's arguments filed October 25, 2004 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection labeled paragraph 2) maintained in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive. The applicants stated that claim 1 was previously amended to provide that the prodrugs are phosphates, carbonates, amino acids or esters. However, the definition of pro-drug in the specification is such that pro-drug refers to "those compounds which are metabolized into compounds of the general formula (I) in vivo".

The term pro-drug is of indeterminate scope in that they vary widely from drug to drug. It is not known which moiety of formula (I) would form the basis for the pro-drug. Every ester and amide in theory is biohydrolyzable, i.e. is capable in some degree of hydrolyses. Not to mention the many in vivo environments that this occurs in. It is the Wands factors, which are used to evaluate the enablement question. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5)

the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant invention has claims, which embrace substituted benzoimidazo[4,5,1-jk][1,4]benzodiazepine compounds. The instant compounds of formula (I) wherein the pro-drugs are not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claims 1-8 and 10-3. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claims 1-8 and 10-13 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

2. With regards to the 35 U.S.C. § 112, first paragraph rejection labeled paragraph 3) maintained in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive. The applicants stated that claim 10 has been amended to delete any reference to "prophylaxis". However, the applicants failed to comment on the enablement rejection with respect to claim 13 and the specific diseases and/or disorders claimed in claim 10. At the time of filing of the present application, the nexus between the Applicants' claimed diseases or disorders and PARP

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inhibitors was not known in the art. While the some of the specific diseases listed in claim 10 have been indicated by the applicants to have a nexus with PARP inhibitors, this does not provide enablement for all of those diseases and/or disorders listed as well as claim 13, which is any and all diseases associated with PARP inhibitors. Treatment of diseases based solely on their efficacious in inhibiting the activity of at least one poly(ADP-ribose) polymerase does not provide for the treatment of every disease and/or disorder claimed herein. Not all diseases and/or disorders are treatable, let alone preventable. There is no evidence that any of the compounds instantly embraced have any one utility generically embraced in claim 13 or specifically recited in claim 10. Where structure sensitivity exists (in the pharmaceutical art) degree of testing must be representative of claims' scope. Note *In re Fisher* 166 USPQ 18; *In re Surrey* 151 USPQ 724. Thus the uses being urged are not in currently available form based on the activity relied on and the specification provides only a starting point for further research. Note *Genentech vs. Novo Nordisk* 42 USPQ 2d 1001. It is difficult to treat many of the disorders claimed herein.

Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689. The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "cancer" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally

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effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task.

As stated in the MPEP, 2164.08 "[t]he Federal Circuit has repeatedly held that 'the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971). See also Plant Genetic Sys., N.V. v. DeKalb Genetics Corp., 315 F.3d 1335, 1339, 65 USPQ2d 1452, 1455 (Fed. Cir. 2003) (alleged "pioneer status" of invention irrelevant to enablement determination)."

Claims 10 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

3. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejection labeled paragraph 4a) and 4b) maintained in the last office action, which are hereby **withdrawn**.

4. The applicants' amendments and arguments are sufficient to overcome the objection to claim 12 maintained in the last office action, which is hereby **withdrawn**.

5. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, first paragraph rejection labeled paragraph 8a) and 8b) of the last office action, which are hereby **withdrawn**.

6. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejection labeled paragraph 9 a), b), c), d), e), f), g), h), l), j), k), l) and m) of the last office action, which are hereby **withdrawn**.

In view of the amendment dated October 25, 2004, the following new grounds of rejection apply:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claims 1, 2, 4-8 and 10-13 are vague and indefinite in that it is not known what is meant by the definition of w where w is a letter O. It is believed that the applicants intended the numeral 0.
- b) Claims 1-4, 8 and 10-13 are vague and indefinite in that it is not known what is meant by the definition of E where E is  $\text{-NHCOCHX}^4\text{-}$ . The carbon atom of the CH group is not valence satisfied, i.e. only has three bonds  $\text{-N(H)-C(=O)-CH-X}^4\text{-}$ .
- c) Claim 6 is vague and indefinite in that it is not known what is meant by the definition of  $\text{R}^4$  where  $\text{R}^4$  includes the moiety  $\text{Fo-1}^2$ . It is believed that the applicants intended  $\text{G}^1\text{-F}_{0,1}^2\text{-G}^2\text{-G}^3$ .
- d) Claim 6 recite the limitation " $\text{F}^1$ " in the definition of  $\text{R}^4$ . There is insufficient antecedent basis for this limitation in the claim.
- e) Claim 7 recites the limitation " $\text{F}^1$ " in the definition of  $\text{R}^4$ . There is insufficient antecedent basis for this limitation in the claim.
- f) Claim 10 is vague and indefinite in that it is not known what is meant by the list of diseases and/or disorders which is not stated in the form of a proper Markush grouping.
- g) Claim 11 is vague and indefinite in that it is not known what is meant by the structure of formula II where B is bonded to the H atom.
- h) Claim 11 is vague and indefinite in that it is not known what is meant by the structure of formula III where the  $\text{NH}_2$  in the ring is not valence satisfied, i.e. the nitrogen atom has four bonds.




- i) Claim 12 is vague and indefinite in that it is not known what is meant by the variable Y in formula IV where Y is a mono-valent substituent on the ring, however, Y as defined in claim 1 is divalent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Brenda L. Coleman  
Primary Examiner Art Unit 1624  
January 31, 2005